PMSD/ISB

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Follow-up to Methyl Bromide Registration Standard. Methyl Bromide Industry Panel Response (9/22/88) to DEB Review of 7/14/88 on Postharvest Protocol, Analytical Methodology, and Storage Stability. RCB No. 4399.

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and

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and

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Background

The Methyl Bromide Industry Panel (MBIP) had submitted protocols covering the types of chamber to be used, the analytical methodology, and storage stability studies. An interim metabolism study had also been submitted. The present submission consists of MBIP's response to DEB's review of 7/14/88 and a request for a conference as soon as possible.

Summary of Remaining Protocol Issues (For further discussion, see the Detailed Considerations Section of this review)

1. The contribution of MeBr and any volatile metabolites to the total radioactive residue should be taken into account.

2. DEB agrees that it would be difficult to determine the presence of 5-bromouracil with ^{82}Br as a probe. The registrant will need to determine whether 5-bromouracil is present chromtographically, by LC/MS, or by any other appropriate methodology.

3. The registrant will need to adhere more closely to Good Laboratory Practices (GLP). According to GLP guidelines, all changes in the notebook should be initialed, dated, and explained.

4. Standard curves should not be generated on log/log paper.

5. Standard curves should cover the range of residue levels determined in the commodity.

6. Determining residue levels by a comparison with the response from one injection is not appropriate.

7. The conversion of ppm MeBr (v/v) to ppm MeBr (w/w) should be explained; some discrepancies, discussed more fully in the text of this review, also need to be resolved.

8. The registrant needs to describe any precautions taken during chopping and compositing to prevent loss of MeBr.

9. The ion selective electrode method appears to be too erratic for the generation of residue data; recoveries exceeding 170% were found in wheat, rice, and strawberries.

10. Decline curves to cover the storage period from sampling to analysis are needed for each commodity.

11. The registrant will need to support his contentions regarding commercial practices with documentation.

12. Data on waxed and unwaxed commodities are needed. If it can be shown for three different crop groups that waxed commodities represent the worst case, then only data on waxed commodities are needed. If the registrant opts to revise the label to permit the fumigation of unwaxed commodities only, he will need to show that this restriction is practical.

13. If interstate commodities are not to be fumigated, why are these uses being supported? If the treated commodities may be diverted to domestic use, the appropriate residue data

are needed.

14. The temperature of the chamber, the commodity itself, and the aeration temperature should reflect the worst case expected in commercial practice.

15. Residue data on grain dust are needed.

16. The residue data should include representative samples of bruised or stemless fruit.

Recommendations

DEB recommends that the registrant modify the protocols to include the issues summarized above; deficiencies cited in earlier memos should also be addressed.

Detailed Considerations

DEB's Comments/Conclusions from its 7/14/88 review will be restated or paraphrased under the appropriate heading, followed by the registrant's response, and DEB's Comments/Conclusions.

Metabolism Studies

Review of 7/14/88 (memo of C. Deyrup)

DEB had not had a chance to review the protocol used in the metabolism studies.

Registrant's Response

The registrant claims that a "study plan" was sent to the Agency on 2/12/88, although a formal protocol was not sent.

DEB's Comments/Conclusions

DEB has search its files and requested RD (W. Francis) to search its files. Unfortunately, no copy of the study plan could be found. DEB regrets any inconvenience this loss may have caused the registrant.

Review of 7/14/88 (memo of C. Deyrup)

Metabolism studies should be aimed at delineating the total radioactive residue (TRR), including the contribution of parent and volatile metabolites. The crop samples had apparently been subjected to drying in an evacuated desiccator, lyophilization, and/or Soxhlet extraction before counting.

Registrant's Response

The MBIP desires to meet with the Agency on the issue of distribution and composition of the total radioactive residue.

DEB's Comments/Conclusions

As DEB pointed out in its 7/14/88 review, the metabolism study addressed the identity of bound residues only. The contribution of MeBr and any volatile metabolites was not determined. This deficiency remains unresolved.

Review of 7/14/88 (memo of C. Deyrup)

DEB agreed to MBIP's suggestion at the meeting of 10/15/87 that a corn metabolism be carried out with ^{x}Br.

Registrant's Response

The registrant has submitted a memo from Dr. E.J. Bond (Research Centre, Agriculture Canada), who contends that it is not feasible to conduct metabolism studies on corn using ^{82}Br. The half life of ^{82}Br is only 35.9 hours. Dr. Bond estimated that about 15 days would elapse between the synthesis of $Me^{82}Br$ and the completed analysis of fumigated material. This estimate was based on a period of one week for the synthesis, acquisition, and delivery of the fumigant, 3 days for the treatment of the material, and 6 days for the analysis and identification of the radioactive metabolites. By the time of analysis, Dr. Bond estimated that there would only be 1000 dpm left, if one started out with 10 millicuries.

DEB had been concerned about treatment with MeBr that could lead to the formation of 5-bromouracil. Dr. Bond suggested that if this compound is of concern, it could be sought chromatographically.

DEB's Comments/Conclusions

Dr. Bond's estimate of the time needed to carry out the metabolism study appear to be quite conservative. DEB agrees that at least 15 days would elapse between acquisition of the ^{82}Br and the final analysis and identification of ^{82}Br-containing residues. Therefore, DEB agrees with the registrant that the ^{82}Br metabolism study is not feasible.

DEB agrees that it would be difficult to determine the presence of 5-bromouracil with ^{82}Br as a probe. The registrant will need to determine whether 5-bromouracil is present chromtographically, by LC/MS, or by any other appropriate methodology.

Review of 7/14/88 (memo of C. Deyrup)

The review of 7/14/88 also made the following points in reference to the metabolism study interim report. These issues were not addressed in the present submission and are not resolved.

DEB suggested that the petitioner investigate the distribution and composition of the TRR as a function of aeration time.

DEB asked that the registrant clear up several technical details of the study.

Residue Analytical Methods

MeBr Analysis--Review of 7/14/88 (memo of C. Deyrup)

DEB had observed that the latest revision of the MeBr analytical method related the amount of water added to the sample and the GC oven temperature to the commodity. Other modifications were enumerated, and DEB recommended that the modifications be published in the Pesticide Analytical Manual, Vol II as a letter method, if the requested validation data were adequate.

DEB also suggested that the registrant include a summary at the beginning of the text to explain that the water determination is essential for the iBr analysis.

Registrant's Response

The same oven temperature (75°C) is used for all analyses and is satisfactory for most analyses. Initially the oven temperature was changed to separate MeBr from background. Under normal circumstances, a temperature of 75°C is recommended.

The registrant emphasizes the importance of preparing standards with the same volume of water used for preparing test samples. [The construction of standard curves involves the spiking of check samples.] The registrant advises that the volume of water added range from 100-250 ml; if more than 250 ml are required, the weight of the sample should be reduced.

The registrant considers the modifications to be "very minor," so that the revised method is essentially the same as that validated by the EPA.

The petitioner has submitted a revised Procedure I (MeBr by Headspace GC). The text begins, "Note: the inorganic bromide (iBr) concentration (procedure 2) can be generated from the same blended sample after it is used to determine the methyl bromide level in the commodity.

The water content of the sample must also be known prior to calculation of the iBr concentration in the sample."

DEB's Comments/Conclusions

DEB agrees with the registrant that the method is essentially the same as the method validated by the EPA. Revised methods may be published in PAM II as letter methods to aid the analyst. When this is done, the letter method is not subjected to another

method validation at the Beltsville laboratory. In this case, once the necessary validation data have been reviewed, DEB would recommend that the revised method be published because the information on the water volume, the possible need for changing the temperature, and the longer blending period would all be useful to a chemist attempting the analysis.

The rewritten Procedure I (analysis of MeBr) explains that iBr can be analyzed from the same blended sample used to determine MeBr, but that the water content of the commodity must first be determined. Procedure I has been adequately revised.

MeBr Analysis--Review of 7/14/88 (memo of C. Deyrup)

MBIP will need to submit fortification/recovery data and sample chromatograms to validate the residue data.

Registrant's Response

The registrant explains that fortification/ recovery data are provided by the use of the standard addition technique for constructing the standard curves. The registrant has submitted raw data sheets, chromatograms, and standard curves, and has left the task of estimating the percent recoveries to DEB.

DEB's Comments/Conclusions

DEB has the following general questions regarding the submitted raw data.

1. There is a column headed "Concen." on the data sheets for the MeBr analyses used to generate the standard curves. All the entries in this column have been crossed out at least once, and another column, "Adj ppm" has been added. According to GLP guidelines, all changes in the notebook should be initialed, dated, and explained.

   In a telecon with Dr. Duafala [Trical (a member of the MBIP), 10/14/88), DEB was informed that the crossed out figures represented ppm MeBr on a v/v basis. Dr. Duafala indicated that this sort of data presentation was not appropriate; He said that a written explanation and recalculation of the "Adj ppm" would be submitted.

   DEB agrees that, in this case, the use of the standard addition technique does provide recovery data. In order to construct the standard curves, MeBr is added to the commodity and water in the blender jar before blending. Therefore, each point on the curve represents an analysis of a fortified check sample. DEB has estimated the percent recoveries from the submitted standard curves. The recoveries are given below:

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Commodity	Fortification level (ppm)	% Recovery
Carrots	0.17-14.30	84-126
Potatoes	0.04-18.90	88-116
Walnuts	69.74-182.0	98-147
Wheat	0.34-14.24	79-112

The registrant needs to explain the relationship between "Adj ppm" and the original entries. Calculations converting the original entries (based on v/v ppm) to the adjusted ppm should also be submitted.

2. The standard curves were graphed on log/log paper. Since this is a departure from the usual practice, DEB regraphed data from carrots and wheat on linear paper. Although a linear relationship was achieved on log/log paper, parabolas resulted when linear paper was used. DEB checked with Ron Thomas (ACS, BUD) who said that the electron capture detector (ECD) was probably being saturated at the high fortification levels employed. The ECD is most reliable in the initially linear section of the standard curve before the curve begins to plateau. Even if the standards bracket the residue values, residue levels are difficult to determine after the curve begins to plateau because the greatly decreased slope leads to a greatly decreased sensitivity. Estimating residue levels from standard curves graphed on log/log paper would not be acceptable for generating residue data. However, for the purpose of the study, which was to examine relative levels resulting from fumigation under a tarp, or in a room, chamber, or vacuum chamber, DEB concludes that the log/log standard curves are adequate.

3. The standard curve for walnuts fumigated in a chamber would not be acceptable for generating residue data. The raw data consist of 5 determinations, which ranged from 0-182 ppm. One determination was of an unfortified sample; so of course this point could not be plotted on the log/log paper used to construct the standard curves. Another point was omitted, and two points were virtual duplicates (93.90 and 94.18 ppm). This curve essentially represents a line drawn through two points.

   DEB can conclude that this standard curve may be used to estimate relative amounts of MeBr; the vacuum chamber fumigation did result in higher residue levels than the tarpaulin fumigation.

4. Since the crossed out residue levels represent ppm MeBr (v/v), DEB expected that the average of these values for any one test would correspond to the average value reported in the original submission. This does not appear to be the case. See below. The original mean was calculated from the average of the crossed out values on the raw data sheets of the current submission.

Commodity	Mean MeBr Concentration			
	Tarp	Room	Vault	Vacuum
Carrots (1/20/88)	10.14	146.94	160.2	173.0
Original mean	10.94	155.4	170.3	197.0
Potatoes (1/20/88)	0.011	130.8	296.4	403.6
Original mean	0.113	134.1	355.9	385.4
Walnuts (1/20/88)	243.4	551.3	559.5	819.5
Original Mean	310.5	606.7	614.2	758.6
Wheat (1/20/88)	0.498	5.79	5.35	14.42
Original Mean	1.33	10.94	10.11	16.40

The registrant will need to explain why the originally submitted mean levels, expressed on a ppm (v/v) basis, do not appear to be in agreement with the average of the crossed-out values in the present submission; according to Dr. Duafala, these values are also expressed on a ppm (v/v) basis.

5. The registrant should also explain how the standard curves are used to obtain the residue levels. For instance, in the wheat vacuum chamber study, a residue level of 0.7637 ppm was reported. From the vacuum chamber standard curve, DEB estimates that the level would be 0.63 ppm. Was a different standard curve used?

MeBr Analysis--Review of 7/14/88 (memo of C. Deyrup)

DEB asked the registrant to describe any precautions taken during maceration of the sample to prevent loss of MeBr.

Registrant's Response

The samples are blended in a closed, air tight system; so it should not be necessary to measure MeBr loss during maceration.

DEB Comments/conclusions

Step 2 of Procedure 1 instructs the analyst to "Chop up commodity to be analyzed." DEB is concerned that during chopping and compositing, MeBr residues could be lost. This deficiency is not yet resolved.

iBr Analysis--Review of 7/14/88 (memo of C. Deyrup)

The description of the method should specify if the ion selective electrode (ISE) can be attached to an ordinary pH meter.

Registrant's Response

The electrode can be connected to any pH meter capable of mv or direct concentration readout. The Corning PC-310 was used in the MBIP study.

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DEB's Comments/Conclusions

This deficiency is resolved.

iBr Analysis--Review of 7/14/88 (memo of C. Deyrup)

The description of the method should be rewritten so that the operations and calculations are more comprehensible, and MBIP should verify that the submitted equation is correct.

Registrant's Response

MBIP has submitted a revised description of the iBr methodology and has corrected the equation.

DEB's Comments/Conclusions

The revised description is much easier to understand than the original version. However, there are two confusing typographical errors in the summary preceding the step-by-step instructions. After an aliquot of the extract is transferred to a beaker, the summary continues, "A three pint standard addition is then performed to the extract sample just tested. A linear regression is performed on the 4 pounds and an initial solution concentration (corrected for recovery) is calculated." The registrant will need to correct the summary. This deficiency is not yet resolved.

iBr Analysis--Review of 7/14/88 (memo of C. Deyrup)

DEB suggested that a sample calculation of iBr should be included in the revised version to illustrate the use of the graph and equation. DEB also needed fortification/recovery data to validate the method and to support a limit of determination.

Registrant's Response

MBIP has submitted the correct equation for determining the ppm iBr in the raw commodity and has carried out a sample calculation illustrating the use of the equation. Dr. Duafala of Trical informed DEB that graphs were not actually plotted; the meter readings and iBr concentration were entered into a computer which carried out a linear regression to give the iBr concentration of the test sample (telecon, 10/14/88). The recoveries from each standard addition were also calculated for each point by the equation:

$$\% \text{ Recovery} = \frac{\text{Conc after add'n-Conc preadd'n}}{\text{Conc added}} \times 100$$

With additions of 8.6 to 48.35 ppm, the following recoveries were reported.

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Crop	% Recovery
Wheat	117.8-173.9
Carrots	92.3-98.4
Potatoes	71.4-84.1
Walnuts	73.4-80.6
Rice	103-186
Walnuts	110-149
Strawberries	89.3-187

In order to demonstrate the limit of determination, MBIP has submitted a standard curve for iBr in water; fortification levels ranged from 0.799 ppm to 79.9 ppm. The instrument response was linear throughout the range tested; linear graph paper was used.

DEB's Comments/Conclusions

The only standard curve submitted reflected the addition of iBr to water. Even though the standard-addition technique should theoretically compensate for matrix effects, DEB is not convinced that the ISE method is adequate because of the wide range of recoveries reported. In one commodity, strawberries, the reported recoveries ranged from 89-187%. A residue level of 21,890 ppm iBr (also in strawberries) provides further evidence of problems with the ISE method. DEB considers such a range as too imprecise to determine residue levels.

Storage Stability Study---Review of 7/14/88 (memo of C. Deyrup)

No recovery data or standard curves were submitted.

Registrant's Response

The registrant has submitted representative chromatograms of MeBr analyses, standard curves (MeBr), recoveries of iBr, and has reported a recovery of 92% for rice.

DEB's Comments/Conclusions

The MeBr standard curves were plotted on log/log paper. The highest fortification level in the standard curve for rice was about 0.6 ppm, for walnuts, about 0.4 ppm, and for strawberries, about 0.2 ppm. The highest level reported in rice was about 0.7 ppm; this level is at least within an order of magnitude of the fortification levels in the standard curve. However, the MeBr levels in strawberries ranged up to 49 ppm, and the levels in walnuts ranged up to 221 ppm. Since the submitted standard curves didn't cover the residue levels found, the MeBr levels in these commodities were apparently estimated from the height or area from a sample spiked at an appropriate level. This technique is equivalent to estimating residue levels from a 1-point standard

curve and is not adequate for determining residue levels.

Recoveries from each crop should be reported.

DEB concludes that the methodologies (MeBr and iBr) used in the storage stability study are not adequate.

Storage Stability Study---Review of 7/14/88 (memo of C. Deyrup)

It is necessary to generate a decline curve to cover the storage period from sampling to analysis for each commodity. The rate of dispersion of the gas from the samples could be governed by the amount of wax on the surface, the surface to volume ratios, maturity of the commodities, storage time before fumigation, etc.

Registrant's Response

Commodities are being analyzed as soon as physically possible after aeration. All analyses are performed within 24 hours of fumigation. Fumigated foods do not reach the consumer for at least 24 hours after fumigation and are shipped at about 40°F. MBIP contends that it is measuring a worst case residue level.

DEB's Comments/Conclusions

Commodities may be monitored by the FDA as soon as they enter interstate commerce. Therefore, DEB must be able to estimate the residue level of the commodities at that point. If commodities lose MeBr under the storage conditions before analysis, the extent of loss must be known so that DEB can recommend an appropriate tolerance level.

DEB has learned that wax does affect the MeBr dispersal from apples; the other factors mention by DEB in its 7/14/88 review could also affect the dispersion of the gas from the samples. The rate of dispersion from one commodity may not be applicable to others. Therefore, DEB concludes that storage stability studies are needed for each commodity.

Storage Stability Study---Review of 7/14/88 (memo of C. Deyrup)

DEB wanted to know why an FID detector was used in the storage stability study when even higher levels of MeBr were determined with an ECD detector in the investigation of different chamber types.

Registrant's Response

MBIP explains that the representation of residue levels in terms of ppm (v/v) apparently confused RCB. From now on, all data will be expressed in terms of ppm (w/w). The FID was used in the storage stabiity study because residue levels exceeded 1 ppm.

DEB's Comments/Conclusions

DEB discussed the detector problems with R. Thomas at the EPA's laboratory in Beltsville (BEAD). In the chamber study, parabolic standard curves were obtained when the data were regraphed on linear paper. According to Mr. Thomas these parabolic curves indicate that the ECD was also reaching saturation in the chamber study. Mr. Thomas said that an FID would not be the detector of choice for MeBr because of its lack of selectivity; also, since MeBr only has one carbon, the FID is not particularly responsive toward MeBr.

The registrant will need to submit an explanation of what was meant by ppm (v/v) and will need to submit calculations converting ppm (v/v) to ppm (w/w).

Parameters which may Affect Post Harvest Fumigation--Review of 7/14/88

If it is the petitioner's intent to permit vacuum chamber fumigation, residue data reflecting vacuum chamber fumigation are required. MBIP has the options of restricting vacuum fumigation to only those crops where vacuum fumigation is of use and generating residue data on these crops, or of eliminating vacuum chamber treatment from the label altogether.

Registrant's Response

MBIP will generate data for those commodities which require vacuum chamber fumigation and will revise the label to include vacuum chamber fumigation for only those crops for which data have been submitted.

DEB's Comments/Conclusions

DEB concludes that this approach will provide adequate residue data.

Parameters which may Affect Post Harvest Fumigation--Review of 7/14/88

Some data reflecting the fumigation of trucks, trailers, or vans should be submitted. Data in RCB's files indicate that residues may be higher after the fumigation of trucks.

Petitioner's Response

Residue levels are a function of dose, sealing, and nature of the commodity being treated. This item should be discussed at a meeting between the EPA and MBIP.

DEB's Comments/Conclusions

DEB concludes that it may not be necessary to provide data from commodities fumigated in trucks. The preliminary data indicating

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that higher residue leels would result from fumigating commodities in trucks were in error.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

1. RCB's guidelines as put forth in its review of the almond protocol (memo of W. Hazel, 11/3/87), apply to all residue tests. The tests should be conducted at maximum label rates and represent actual commercial fumigation events in all respects, such as MeBr introduction, temperature, humidity, air circulation, packaging, load factor, and aeration and storage conditions. For example, grapes may be packaged in lugs containing wood shavings, which, according to the APHIS plant protection manual, are highly sorbent. Also, many commodities are stored cold after fumigation. Moreover, the residue data should reflect the range of temperatures expected during fumigation, or MBIP should demonstrate that the fumigation temperatures chosen represent the worst case. RCB notes that the APHIS manual uses lower rates with higher fumigation temperatures, but there is no tie-in of the rate and the fumigation temperature on the label submitted

Registrant's Response

The registrant wants to discuss all these issues at a meeting.

DEB's Comments/Conclusions

These issues remain outstanding.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

2. MeBr levels should be monitored in various parts of the loaded vault before sampling. Load factors typical of commercial operations should be used.

Registrant's Response

"Monitoring of fumigant level inside the chamber is irrelevant to this project. We are measuring residues in raw agricultural commodities and in foods "as consumed." The ratio of fumigant to commodity w/w increases as the load factor decreases. Reduced load factors should give a worse case picture."

DEB's Comments/Conclusions

Because the MeBr levels in a fumigation chamber decrease as the commodities sorb the gas, monitoring of the MeBr levels in the chamber may be carried out during the fumigation. For instance, in the Plant Protection and Quarantine Treatment Manual (PPQ), the treatment for deciduous fruits is given as:

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"24 g/m^3 (1.5 lb/1000ft^3) for 2 hours at 26.5-31.5°C

(19g (oz) minimum gas concentration at 1/2 hour)
(14 g (oz) minimum gas concentration at 2 hours)"

It is true that smaller load factors would present the worst case, however, the load factors for the residue studies have not yet been specified. The registrant needn't monitor levels of MeBr in the chamber, provided that:

1. The load factors employed are relatively low (R. Sell, USDA/ARS, recommends <10%, using the APHIS definition of load factor), and

2. Samples are taken from all areas of the chamber and are composited before analysis. The samples should also be drawn from the top, middle, and bottom of the containers.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

3. Many commodities are waxed. Where appropriate, residue data should be generated on waxed and unwaxed commodities.

Registrant's Response

The issue of waxed Florida citrus will be addressed. MBIP also states, "The words "where appropriate" are significant. Most of the commodities listed are not fumigated for interstate shipments. Imported fruits or vegetables are not waxed prior to treatment. Export fruits are not subject to these regulations"

DEB's Comments/Conclusions

Since apples are waxed, DEB contacted the International Apple Institute (Mr. Derr) and the Northwest Horticulture Council (Mr. C. Schlect), who both said that the ongoing residue trials were being carried out so that apples could be exported to Japan. Under the present conditions, MeBr would not be used on domestic apples. DEB contacted Dr. H. Moffitt (ARS/USDA), who is overseeing the apple trials. Dr. Moffitt said that there is a chance that the treated apples could be diverted to domestic use, as these apples are not reserved for Japan only and are not owned by Japan at the time of treatment.

Dr. Moffitt said that the effect of waxing had been investigated. Waxed apples take up MeBr at a slower rate than unwaxed apples, and also release the sorbed MeBr at a slower rate. Higher residue levels were found in waxed apples after fumigation and aeration. As a result, the use for Japan stipulates that MeBr be applied only to unwaxed apples. The apples may only be waxed 10-14 days after fumigation. The apples are stored at 2°C during this time.

These results underscore DEB's concern on the effect of waxing. The registrant will need to furnish residue data on waxed and

unwaxed commodities for each of the residue trials involving crops which may be waxed. If it can be shown that the waxed commodities represent the worse case in at least 3 different crop groups, residue data on waxed commodities only may be submitted. If the registrant proposes to revise the label to limit fumigation to unwaxed commodities, he will need to support the position that this restriction is practical by documentation.

In generating the residue data on waxed commodities, the registrant should be aware that different kinds of waxes are used. For instance, Dr. Moffitt said that two types of waxes are used on apples. He said that the two waxes, carnauba and shellac, may affect residue levels differently.

DEB notes that the schedule used for apples intended for export is different from the schedule for the apple protocol; the dosage rate is 3.5 lbs/1000 ft^3, instead of 3 pounds. If the label submitted with PP #5F3300 is intended to cover this use, the registrant will need to revise the label.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

4. The residue data should encompass a range of sizes of a commodity. For example, data on both tomatoes and cherry tomatoes should be generated.

Registrant's Response

Interstate tomatoes are not fumigated. Samples for analysis will include a range of fruit sizes to give a representative value.

DEB's Comments/Conclusions

The registrant needs to clarify the proposed use. If interstate tomatoes are not to be fumigated, why is the use being supported? If treated tomatoes may be diverted to domestic use, separate residue data on both large and small tomatoes are needed because they travel separately through interstate commerce.

The registrant states "Samples for analysis will include a range of fruit sizes to give a representative value;" does this mean that cherry tomatoes will be sampled separately?

Other Factors in Generating Residue Data (Numbering of 7/14/88)

5. Residue data reflecting multiple applications are required when appropriate. MBIP will need to explain how it determined the number of applications for each commodity.

Registrant's Response

This will be done.

DEB's Comments/Conclusions

The registrant should support the explanation with documentation.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

6. If certain commodities are generally stored before fumigation, some of the residue data should reflect representative storage periods and temperatures before fumigation.

   It has been reported in the literature that the storage temperature prior to fumigation may affect the amount of fumigant absorbed by the commodity.

Registrant's Response

The registrant concedes that the temperature of the commodity at the time of treatment affects the amount of fumigant absorbed. The registrant states, "Studies will be run at temperatures of the commodity, as normally treated."

The temperature of the commodity is a function of the storage temperature, not the storage period.

DEB's Comments/Conclusions

Both the temperature of the chamber and the temperature of the commodities should reflect the worst case expected in commercial practice.

DEB did not believe that the temperature of the commodity was a function of the storage period. Rather, it seemed to DEB that after long periods of storage, the permeability of the commodity could change due to drying, cracking of the skin, thinning of the skin, etc. DEB has contacted Dr. H. Moffitt (USDA/ARS) and learned from him that residue levels in apples with closed or open calyxes were similar. Therefore, although changes do occur during storage, Dr. Moffitt felt that any change in the skin during storage would probably have little effect on residue levels. Dr. Moffitt said that the major parameters affecting residue levels were the temperature and the presence of added wax.

DEB concludes that residue data reflecting representative storage periods will not be required.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

7. If certain commodities are generally picked green, the residue data should reflect residues in both green and mature fruit. Sinclair and Lindgren (see above) reported that the amount of fumigant sorbed by the commodity could depend upon its stage of maturity.

Registrant's Response

The commodities will be treated at the stage of development during which fruit are treated commercially

DEB's Comments/Conclusions

DEB's concerns on the effect of maturity on residue levels are satisfied.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

8. The use of MeBr in grain elevators could lead to higher residue levels in grain dust than in the grain itself. Grain dust is a cattle feed item. Therefore residue data on grain dust are also required.

Registrant's Response

Any methyl bromide in dust would dissipate during blending and/or storage. Grain in silos is not treated unless it is intended for processing or export. Under these circumstances, the dust is not used for cattle feed.

DEB's Comments/Conclusions

DEB has contacted D. Krejci (Grain Elevator and Processing Society or GEAPS) and T. Klevay (Miller's National Federation). Both Mr. Krejci and Mr. Klevay said that silos would generally not be treated unless there was an infestation problem, in which case, the silos would probably be treated with aluminum phosphide. Phosphide is cheaper, and the use of MeBr requires the use of special recirculation equipment. However, MeBr may be used because of time constraints (MeBr is faster than AlP which must decompose to give the toxic fumigant PH_3).

Mr. Krejci said that the grain would be treated when it is infested, regardless of what its ultimate destination may be, and the destination of the grain has no effect on the disposal of the grain dust. Since the two uses of grain dust are as a landfill and as a cattle feed, it is probable that dust treated with MeBr would be used as cattle feed.

Mr. Klevay said that he knew of only one company that uses MeBr on the grain itself, although MeBr is often used as a structural fumigant. I asked whether this company would use the grain dust from treated grain as a landfill or whether the dust would be added back to the feed stream. He said that it would not be used as landfill, and would probably be added back to the feed stream. Since Mr. Klevay said that he had reviewed the wheat protocol covered in DEB's memo of 9/23/88, DEB asked him if grain dust data could be generated. He said that they would have to use the equipment at hand, and this is apparently quite large. The pneumatic

grain dust collectors are located at various points in the pathways of the storage system and collect dust from all the elevators. The collected dust would not have originated from one treated elevator. However, Mr. Klevay said that cleaning house equipment should be capable of separating the dust from the grain. DEB told him that the grain dust analyzed should conform to commercial grain dust from elevators, and the wheat grain should be analyzed before cleaning. DEB consulted K. Goforth (GEAPS) who said that the chaff does not need to be separated from the fines; commercial grain dust consists of fines and chaff.

DEB concludes that residue data on grain dust need to be generated; without data DEB cannot be certain that the MeBr would dissipate as the registrant contends.

DEB has learned that food grade mineral oil may be added to grain at a 200 ppm rate in order to minimize grain dust concentration in the air. Since DEB has also learned that added wax doe affect the rate of MeBr dispersion from apples, there is concern that the added oil may also affect the dissipation of MeBr residues from grain. Therefore residue data are needed on wheat grain which has been treated with mineral oil and on dust from this grain.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

9. The residue data should reflect the analyses of a representative proportion of bruised or stemless commodities. Data in RCB's files indicate that certain fumigant levels are higher in such fruit.

Registrant's Response

Bruised and stemless fruit are not sold or consumed. Any such items in our program will result in a "worst case" situation which is protective of public health.

DEB's Comments/Conclusions

Bruised and stemless fruit are sold and consumed. According to P. Manol, USDA Marketing Inspection, Fresh Products Branch, in the absence of other defects, 12% of table grapes may be "shattered berries" (stemless), 10% of US #1 peaches may be bruised, and 10% of US #1 apples may be bruised. These standards vary from commodity to commodity. DEB reiterates that the analytical samples contain a representative amount of bruised and stemless fruit.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

10. If tolerances are proposed on the basis of residue levels following a period of aeration, MBIP will need to demonstrate that the aeration period is appropriate (i.e., that the commodity will not be available for sampling by the FDA before the aeration period has elapsed).

Registrant's Response

"This is true."

DEB's Comments/Conclusions

The registrant should note that the aeration period should also be long enough so that the commodity may not be bagged before this period has elapsed.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

11. Samples to be analyzed should be taken from different sections of the container.

Registrant's Response

The registrant intends to select samples from different sections of the container.

DEB's Comments/Conclusions

The registrant should be sure to include some samples from the bottom of the containers, since MeBr is heavier than air.

Other Factors in Generating Residue Data (Numbering of 7/14/88)

12. The aeration temperatures should be specified. RCB suggests that the coolest feasible temperatures for each commodity be investigated. MBIP has the option of revising the label to specify a minimum aeration temperature if it can demonstrate that such a label restriction is practical.

Registrant's Response

The selection of the aeration temperature of commodities is based on many factors. Generally, aeration is at ambient and then the commodity is changed to the desired temperature to preserve quality.

DEB's Comments/Conclusions

Studies at the USDA have shown that the desorption rate of MeBr from apples (unpublished results) and cherries (C.R. Sell, N.G. Klag, and A.K. Burditt, Jr., Pestic. Science, 23, 41, 1988) depends upon the pulp temperature. Since the major factor in the desorption rate is temperature, and the tolerance may need to be based on an aeration time, the temperature must be taken into account for each protocol. The aerations should be conducted at the coldest temperatures used commercially; the choice of aeration temperatures should be supported by documentation. For example, if it is necessary to aerate cherries for 2 days at 60°F, the registrant will need to demonstrate that this would not adversely affect the shelf life to the point of impracticality. If it is

necessary to aerate a commodity for 10 days at 36°F, the registrant will need to demonstrate that it is feasible to withhold the commodity from interstate commerce for this period. If aeration is generally carried out at ambient temperatures, the registrant will need to consider the coldest likely temperatures for the aeration of each crop. If the registrant should propose temperature ranges for the aerations, he would need to document that these aeration temperature restrictions are practical in commercial practice.

The type of aeration (either forced or unforced) should be specified in the protocol and on the label. After conversations with Drs. Sell and Moffitt, DEB is convinced that the factors involved in the aeration process are critical in determining MeBr residue levels.

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